

Harris (H. F.)

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A CASE OF DIABETES MELLITUS QUICKLY FOLLOWING MUMPS.

ON THE PATHOLOGICAL ALTERATIONS OF THE SALIVARY GLANDS, CLOSELY RESEMBLING THOSE FOUND IN THE PANCREAS, IN A CASE OF DIABETES MELLITUS.

BY H. F. HARRIS, M.D.,

*Associate Professor of Pathology at Jefferson Medical College; from
Laboratories of the Jefferson Medical College Hospital, Philadelphia, Pa.*

THE writer's attention was first directed to a possible relation between morbid conditions of the salivary glands and those of the pancreas by the history of a patient suffering from diabetes mellitus, the details of which were as follows:

A. W. R., age forty-two, white, a farmer, applied for treatment at the Medical Clinic of the Southern Medical College, Atlanta, Ga., on the 3d of March, 1895. Family history negative. Except an attack of measles when a child, he never remembers having been sick until three years prior to the time he presented himself for treatment, when he had an attack of mumps. About a month after his recovery he noticed that he began to pass more urine than formerly; since this the quantity of urine voided has slowly but steadily increased. He has constant thirst, and eats much more than was his custom before the trouble began. Bowels are irregular; the stools have generally a much paler color than is normally the case; has lost about thirty pounds in flesh; eyesight has

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recently become much worse. He has suffered from a slight degree of salivation ever since he has had this present trouble.

Physical Examination.—Patient is much emaciated. Pulse 88, respiration 28, temperature 98.4° ; tongue shows slight imprint of teeth. There is an eczematous condition of the skin of the face, neck and back. Patellar tendon reflex lost in both legs; elbow reflex greatly diminished. Heart, lungs, liver and spleen normal so far as could be ascertained. During the first twenty-four hours after coming under observation he passed 6,440 cubic centimetres of urine. It contained no albumin, but 4.6 per cent. of glucose; acetone present. This urine contained 57.96 grammes of urea. The saliva contained traces of glucose. Blood examination showed 3,957,500 erythrocytes to the cubic millimetre; white cells normal. There was 95 per cent. hemoglobin. None of the feces could be obtained for analysis. The man returned to the clinic several times, but finally disappeared, and as a consequence his subsequent history is unknown.

With one or two trifling exceptions, this man presented all the usual symptoms of diabetes, and the case is therefore, clinically, of no unusual interest. As he has, however, been previously healthy and the diabetes so rapidly followed the attack of mumps, it appeared not impossible that the latter disease might have in some way induced the former. Since the writer's attention was called to the matter by this case he has seen in literature several references to the fact that diabetes has not infrequently followed mumps. There are many cases on record which prove beyond doubt that chronic alterations in the parotid may follow mumps, but it is quite clear that its destruction as the result of disease is not followed by the symptoms of diabetes in man.

Following the removal of all of the salivary glands in a dog the writer was able to detect slight traces of what was apparently glucose for a period of ten days after the operation. The animal entirely recovered from the effects of the surgical procedure, and two months after was in perfect health. On looking into the literature, it was found that the same experiment had been previously carried out by Reale.¹

This experimenter was able to induce a mild glycosuria in dogs by the removal of the salivary glands, and, furthermore, produced the same condition in dogs where the previous removal of the pancreas had not been followed by its appearance of sugar in the urine. In the same place Reale refers to a case of diabetes which he thought was due to the fact that the patient, who suffered from salivation, would never swallow any of the saliva. It does not, however, seem that the facts at present before us would justify the belief that alterations in the salivary glands alone would lead to a pronounced condition of glycosuria. But the removal of the pancreas, or even the destruction of a part of it, in most cases, is immediately followed by diabetes in many of the lower animals, as has been shown by the brilliant experiments of v. Mering.² Since the publication of Schmackpfeffer's³ thesis on diseases of the pancreas the possibility of an inflammatory condition of this organ being induced by the poison of mumps has been generally admitted, but, unfortunately, there must always remain some doubt as to the true nature of the case to which he referred. The writer has been unable to find another recorded

¹ Congress of Berlin, 1890, Part II, Fasciculus of Internal Medicine, p. 97.

² Ueber experiment. Diabetes, Verhandl. des V und VI Congr. f. inn. Med., Wiesbaden, 1886 und 1887.

³ Dissertatio inauguralis sistens observationes de quibusdam pancreatis morbis, 1817, 26.

instance where a pancreatitis was supposed to have been induced by mumps, and it would therefore appear that the condition, if it occur at all, is extremely rare, or that the symptoms are of such a character that attention is not directed to the diseased organ. Notwithstanding this, when it is remembered that, in addition to the parotitis, adenitis of the sublingual and submaxillary glands, orchitis, prostatitis, ovaritis, mastitis, nephritis, thyroiditis, and inflammation of the cervical lymphatic glands have been sufficiently often observed to make them well-recognized complications of mumps, it certainly would appear possible, nay, even probable, that a gland so closely resembling the parotid as the pancreas would at times be involved. If this be granted, an admission of the possibility that the changes might become chronic, and lead to permanent structural alterations in the viscus, could scarcely be avoided, in view of the frequently reported atrophy of the parotid and testicle following acute inflammation of these glands resulting from mumps.

The writer does not for a moment assume that every case of pancreatic disease is due to mumps, nor, in the present state of knowledge, does it appear to him probable that it is even common, but the facts as above set forth would seem to justify an investigation by those who are in position to give the matter attention.

That functional alterations in the salivary glands very generally occur in diabetes mellitus has long been known, but the condition has received but little attention from the clinicians, and, so far as the writer can find, none at all from the pathologists. Jaret and Niviere⁴ have recently particularly directed atten-

⁴ Des alterations glandes digestives à sucs alcooliques et de leur importance dans les diabètes sucrés : *Revue de Médecine*, December, 1898, p. 973.

tion to the changes in the saliva in this disease, and have claimed for these glands an importance in the diabetic process which they probably do not deserve. It cannot, however, be doubted, as the case—the record of which follows—proves that profound changes sometimes occur in the salivary glands, in every way resembling those found in the pancreas, in diabetes mellitus.

For the clinical details of this case the writer is indebted to Dr. F. A. Packard, under whose charge the patient was while in the Philadelphia Hospital, and for permission to make the post-mortem, to the kindness of Prof. W. M. L. Coplin, during whose service as pathologist the necropsy was made.

J. H., age sixty-three, white, male, a Pennsylvanian, was admitted to the Philadelphia Hospital July 19, 1897.

Clinical Diagnosis.—Diabetes mellitus.

Family History.—Father died of dropsy; mother died of pulmonary tuberculosis.

Personal History.—Patient was always well up to his present illness. He has never used alcohol. About fifteen months before admission the patient noticed that he began to pass more urine than formerly. He drank more water than usual, and his appetite increased to an abnormal degree, notwithstanding which he gradually lost flesh. Five weeks before admission he noticed a dark spot on the inner side of the big toe of right foot; shortly after a purulent discharge began to come from this spot. This area has been very painful.

Physical Examination.—Except the gangrene of the toe, above referred to, the man was physically sound. The urine was examined and found to contain 3.66 per cent. of glucose. A diagnosis of diabetes and diabetic gangrene of the toe was made, and the patient was

placed on proper diet and treatment. From the time of admission until death the patient has remained in the hospital. Although the gangrenous condition of the toe entirely healed in a short time, the patient's general condition gradually grew worse. A few weeks before death there were added to the diabetic symptoms those of pulmonary tuberculosis, which gave the usual signs of such conditions. While in the hospital he passed, on an average, from 3,500 to 4,000 cubic centimetres of urine. He died on January 26, 1899.

Autopsy was made at 2 P. M., January 29, 1899.

Pathological Diagnosis. — Atheroma of vessels of base of brain; tuberculosis and abscess of lung; tuberculous ulcers of lower part of ileum; atrophy of pancreas; atrophy of salivary glands; closure of cystic duct; gall-bladder adherent to duodenum; ulceration through walls of both of these viscera, causing their cavities to communicate.

Post-mortem Record. — Body of a much emaciated male. Skin and mucous membranes pale; post-mortem rigidity slight. On outer portion of right forearm a tattoo-mark of our Saviour undergoing the pains of crucifixion. On section a small amount of fat is found in abdominal wall. The muscles of the abdominal wall are quite pale. In dependent portions of abdominal and pelvic cavities are found small collections of a slightly reddish-yellow fluid. There is coloptosis. Other abdominal viscera in their normal situations.

Lungs fill their cavities well. The left lung is bound to the thoracic wall by old, very tough adhesions. The parts of the pleural cavity which are not obliterated contain 75 cubic centimetres of slightly blood-stained, opaque fluid; with the exception that the right pleural cavity contains only 20 cubic centi-

metres of fluid, its condition is practically that of the left.

The heart is in its normal position. Pericardium normal; it contains 80 cubic centimetres of clear, yellow fluid. Left side of heart is rather firmly contracted; right side moderately so. The subpericardial fat of left ventricle shows mucoid change. Left auricle contains a small amount of clot, — chiefly post mortem. The right auricle contains a large mass of "chicken-fat" clot. Both ventricles contain a small amount of dark, semi-clotted blood. Aortic and pulmonary valves are continent. Right auriculo-ventricular opening admits three fingers, and the left, two. Each of the aortic valves shows a slight amount of thickening; into these areas there is a small amount of calcareous infiltration. Both mitral valves show the same changes which are observed in the aortic; their edges are, however, normal. The heart muscle is quite friable.

Lower two-thirds of the upper lobe of the left lung are in a state of complete consolidation. Substance does not crepitate; it is grayish in color, and sinks when placed in water. In this area there are numerous small cavities, which contain a pus-like material. The lower lobe is normal. Scattered through the right lung are small nodules, varying in size from barely perceptible points to one centimetre in diameter, which contain a pus-like material. The walls of these abscesses are very thin.

Material from these pus cavities from both lungs was subjected to immediate examination by Professor Coplin, with the following results:

The fresh unstained material was found to consist of pus cells, elastic fibres, giant cells — one of which contained five small, centrally placed nuclei — and granular detritus; in addition there were a few cells about twice

the size of pus cells, with very small nuclei and a clear, almost hyaline, protoplasm. Specimens stained by carbol-fuchsin showed the cellular elements, as above mentioned. There were many diplococci surrounded by a clear space, which suggested a capsule. There were also a few bacilli found which had the morphologic peculiarities of tubercle bacilli. Specimens counterstained by Gabbet's methylene-blue solution showed these bacilli red. Carbol-fuchsin specimens also showed chains of cocci which contained five and six elements. Specimens stained by Gram's method showed the organism as above mentioned, and, in addition, several zoöglea masses of cocci. The spleen weighs 180 grammes. The organ is rather flabby and its capsule is wrinkled. The substance is normal in every particular. The adrenals are normal. The left kidney weighs 225 grammes. On section more blood exudes from the organ than is usual. Capsule strips readily. Beneath the capsule and on the convex border of this kidney there are a few minute cysts, which contain a clear, yellow fluid. The substance of the organ is normal in consistence. The cortex appears slightly thinned. The right kidney weighs 190 grammes. In all essential particulars it resembles its fellow. Bladder and ureters are normal. Rectum is normal. The duodenum just below the pylorus is adherent to the under surface of the gall-bladder. Where joined together there is a small opening through the walls of these viscera, about one centimetre below the pylorus, causing their cavities to communicate. There is a very small fistulous tract, which extends from the interior of the stomach to the edge of this opening. This tract is between the muscular coats of the duodenum and the wall of the adherent gall-bladder. The duodenum is otherwise normal.

With the exception above noted, the stomach is normal. Pancreas is very small, weighing only 35 grammes. It is 13 centimetres long, 4 centimetres wide, and about .5 centimetres thick. The surface of the organ is very nodular, and feels quite hard. On section there is more resistance than is usually the case, but the color is normal. When squeezed a minute quantity of clear fluid exudes. Inspection shows the presence of numerous fibrous-like bands running through the organ. There is evident atrophy, and there has evidently been an old interstitial pancreatitis. There is no evidence of carcinomatous or tuberculous change. The duct of the pancreas seems entirely closed a short distance from the point where it joins the bile-duct.

Liver weighs 2,050 grammes. Its substance is apparently normal in every particular.

The gall-bladder contains a small amount of yellowish and very thick material, which is evidently not normal bile. The cystic duct is entirely closed; at the point where it should open into the gall-bladder there is a calculus having a diameter of two centimetres.

The mucosa of the small intestine is very pale. There is a small oval-shaped ulcer in the ileum, four centimetres above the ileo-cecal valve; the edges of the ulcer are smooth and slightly undermined. The floor of the ulcer is grayish in color; the ulceration apparently does not extend deeper than the muscular layer. The underlying serous coat is normal. The long axis of this ulcer, which is longitudinal to the long axis of the intestine, measures 12.5 millimetres in length, and its width is 7.5 millimetres. Above this ulcer there are found in the ileum six other ulcers, resembling the one just described, with the exceptions that they are small, measuring about 2.5 millimetres in diameter, and are practically round.

In the mesentery, near the head of the pancreas, a lymphatic gland is found which is much enlarged. On section the mass is gray in color and quite soft.

Several lymphatic glands presenting the same peculiarities were found in the neck near the right lobe of the thyroid. The thyroid is normal.

The ascending transverse and descending aorta contain numerous atheromatous patches.

Brain weighs 1,330 grammes; it is in every way normal.

All of the salivary glands were removed and found smaller than normal. The right parotid weighs 12 grammes, and the left 10 grammes. The submaxillary glands weigh 4 grammes each, and the two sublinguals together weigh 3 grammes. These weights are in every instance in excess of what the glands really weighed, as it is found on microscopic examination that many of the pieces which were removed contain no glandular structure at all. These glands, particularly the parotids, show the same peculiarities which characterize the pancreas.

From a culture made from the lung a streptococcus was found. In the first culture a few diplococci were found, but they disappeared on plating. From the spleen a streptococcus was obtained, and also the staphylococcus pyogenes aureus. Cultures from other organs negative.

Microscopic examination. — All of the tissues were fixed in Heidenhain's mercury-bichloride solution. Sections were stained in hematoxylin alone and with eosin, carmalum alone and with picric acid, carbol-luidin-blue alone and with eosin, acid orcein, carbol-fuchsin for tubercle bacilli, and by the methods of Van Giesen, Weigert and Sanfelice.

Pancreas and salivary glands: In the present instance the alterations in the pancreas and salivary

glands may be looked upon as the primary and most important of all the changes found, and, for this reason, will be first considered. As the pancreas anatomically belongs to the groups of salivary glands, and as the pathologic alterations are identical in all of these organs, much useless repetition can be avoided by considering them together. Sections taken from all parts of all of these glands show a very marked thickening of the trabeculae which bind the lobules together

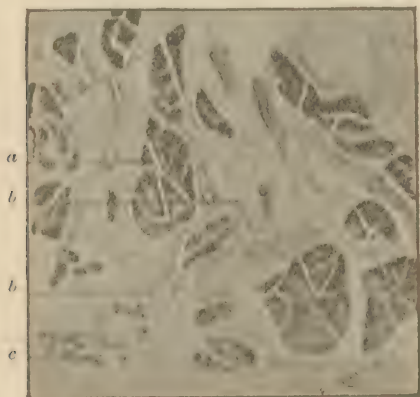


FIG. 1. Section of left parotid under a very low power; carbol-toluidin-blue and eosin; *a*, normal lobules; *b*, greatly thickened trabeculae; *c*, lobule almost entirely changed to fibrous tissue.

(Fig. 1*b*). This thickening is not uniform, the same band being much thicker at some points than at others. In the majority of instances every lobule is separated from adjoining ones by these bands, but here and there two, three or even more lobules lie

practically in contact, and appear in every way normal. The delicate interstitial substance which lies between the individual acini, as a rule, shows no change, but not infrequently this tissue has also become markedly thickened (Fig. 1*c*). In still rarer instances this hyperplastic change has gone on to such an extent that practically all the acini of a lobule have been destroyed, and replaced by newly-formed fibrous tissue. In these areas remnants of the acini sometimes persist as small collections of epithelial cells, closely packed together by the contracting fibrous tissue surrounding them. From what has been said it necessarily follows that the excretory ducts of the glands suffer much, as a result of the pathologic processes, often being greatly reduced in size, and much distorted (Fig. 2*d*). Here also small collections of epithelial cells are often found bearing no resemblance to the normal ducts. Quite a degree of thickening is likewise found in the outer coats of small arteries which lie in the trabeculae (Fig. 2*e*). Scattered through the trabeculae everywhere branched connective-tissue cells are found, and here and there small collections of lymphoid cells, mixed with which are fibroblasts, a few plasma cells and an occasional mast cell. These collections of cells are most prominent around the smaller arteries and ducts, but are also found around some of the smaller veins. Between the acini of some of the lobules considerable collections of such cells are also found; where these cells are present there is always a greater or less increase in the amount of fibrous tissue of the part (Fig. 2*c*). All of the newly-formed tissue consists of white fibrous tissue, there being present in it no elastic tissue fibres. In the trabeculae like collections of cells occasionally occur having no apparent connection with either blood-vessels or ducts, but it is not improbable that many, if not all, of them are

really masses of cells in the vicinity of these structures, the section being, however, so cut that they are not included.

The lymph nodes which were present in these glands in all cases show a decided thickening of their trabeculae. Occupying the periphery of the nodes and ex-



FIG. 2. Section from right parotid; carboltoluidin-blue and eosin. Bausch and Lomb $\frac{5}{8}$ inch. Oc.B. *a*, normal lobules; *b*, thickened trabeculae; *c*, cellular infiltration into a lobule; *d*, a duct the wall of which is thickened and infiltrated with cells, and the lumen decreased in size; *e*, an artery with cellular infiltration into its walls.

tending deeper into their substance are numerous rounded or oblong cells, the largest of which have a diameter of from 9 to 10 μ ; many of the largest cells exhibit no nuclei, the protoplasm is finely granular, and stains intensely with acid dyes. These cells appear to be undergoing degenerative changes. A few of these cells and all of the smaller ones have distinct

nuclei, which are, as a rule, vesicular in character; in some instances the nuclei are elongated and twisted on themselves, much resembling nuclei which are frequently seen in stained blood preparations. The protoplasm of the smaller cells is, as a rule, faintly basophilic, though in some cases it is oxyphilic. Passing toward the central portions of the nodes, still smaller cells are found which are apparently lymphoid cells, the protoplasm of which is somewhat increased in amount; the protoplasm of these cells is almost always strongly basophilic. It seems highly probable that these cells are all derived from the lymphoid cells of the normal nodes. Scattered through the nodes red blood cells are occasionally found. Collections of the larger varieties of these cells are occasionally found in small openings in the tissues, which appear to be dilated lymph channels.

The post mortem, unfortunately, was made so long after death that no reliable conclusions could be drawn as to the condition of the epithelial lining of the acini and ducts. However, a record of the changes observed is not wholly without interest, for, while many of them were doubtless post mortem, others could scarcely have been so.

Sections of a normal parotid in the writer's possession show an average diameter of the acini of from 20 to 25 μ , few being of either a greater or less diameter. Sections of the parotids of the case under discussion show in most instances acini which have diameters varying from 10 to 20 μ . In some instances they are much larger, having diameters varying from 40 to 60 μ ; in these cases several of the apparently swollen acini are generally found together. Acini with diameters intermediate between the former and latter groups are rare. The epithelial cells lining the acini are almost always detached from their basement

membranes, and often they have partially or completely disappeared from the lumina of the acini. The cells themselves are swollen, and their nuclei for the most part no longer take the stain. The protoplasm preserves its power of taking basic stains, but the reaction is not uniform throughout the entire cell, as is the case in normal cells of the kind; in some parts of the cells the protoplasm is abnormally basophilic, while in others the affinity for these dyes is diminished. The protoplasm of these cells is, as is that of the normal cell, finely granular. The cells lining the excretory ducts show the same changes which are observed in those of the secreting parts of the gland. A curious and unexpected find in a bit of muscle attached to the sublingual glands was an encysted trichina.

Lungs: The pulmonary lesions are of a most marked character, and were, undoubtedly, the immediate cause of death. Scattered throughout the lung substance there are numerous miliary tubercles which show the usual caseous centres, around which are very thin walls of fibrous tissue, containing numerous fibroblasts, and here and there typical giant cells. It is evident that in the great majority of instances the tubercles began in the smaller bronchial tubes, but occasionally one is found which clearly began in the air vesicles. Quite frequently small abscesses are also found scattered through the lung substance, and they seemed to have always originated in the smaller bronchi, or, less frequently, in one of the tubercles above referred to. The contents of these abscesses vary somewhat, depending on their point of origin, but all contain multitudes of polymorphonuclear leucocytes, a few swollen epithelial cells, and granular *débris*. The walls of these abscesses are made up of the infiltrated and compressed lung tissue which surrounds them.

Sections stained by Weigert's method show within

them multitudes of streptococci, which morphologically resemble the streptococcus pyogenes. In the sections examined none of the lung structure was normal, the lumina of the air vesicles containing many swollen epithelial cells, a few white blood cells, and an occasional red blood cell; in addition to this there is always found a quantity of granular detritus, and many diplobacilli, which morphologically and in their microchemic properties resemble the micrococcus lanceolatus. Here and there an air vesicle is found which contains many leucocytes, a few swollen epithelial and red blood cells, all of which are bound together by shreds of fibrin. The epithelial linings of the bronchial tubes are for the most part gone, and the tubes generally contain large numbers of polymorphonuclear leucocytes. The arteries of the lung generally show a beginning endarteritis, there being between the inner and middle coats small collections of lymphoid cells. The trabeculae of the lung are greatly swollen and contain rather diffuse collections of swollen connective-tissue cells, lymphoid cells, red blood cells, and a few polymorphonuclear leucocytes, lymphocytes and plasma cells.

Intestine: Sections of the ulcer show that the ulceration extends down to the circular muscular coat. The edges of the ulcers are undermined, and there are found, especially in the submucosa in the vicinity, many typical tubercles. The tissues near the ulcers are infiltrated with lymphoid cells, swollen connective-tissue cells, many mast cells and a few plasma cells. The subperitoneal tissues show some thickening.

Lymphatic glands: Sections of the enlarged lymphatic gland from the abdominal cavity and from those taken from the neck show in every instance typical tuberculosis.

Kidneys: The epithelial cells of the tubules are slightly irregular in form at their free ends, and often

their nuclei stain very faintly or not at all, but they are attached to their basement membranes in the usual way, and, before death, were evidently practically normal. The blood-vessels throughout the kidney contain more blood than is generally found in these organs when normal. There are no other changes.

Microscopic examination of sections from the liver, spleen, stomach, adrenal, testicle, prostate, thyroid gland, brain, and pineal gland showed all of these organs to be normal.

Summary.—Diabetes may follow mumps so quickly that there is at least a strong suspicion that the former disease may be induced by the latter. It is not probable that the diabetes is the result of changes produced in the salivary glands, but their removal in dogs is followed by a slight glycosuria.

On account of the close resemblance in structure between the salivary glands and the pancreas, it would seem probable that a general disease, like mumps, which causes changes in the one, would at times likewise produce alterations in the other.

There is no well-authenticated case of pancreatic inflammation having followed mumps, but in, at least, one instance there is a suspicion of it having done so. Inflammatory changes having once been set up in the pancreas, all analogy would lead to the conclusion that in some instances they might become chronic, and that serious alterations in function would result.

Disturbed functional activity of the pancreas, if marked, probably in all cases leads to diabetes. Alterations in the pancreas and salivary glands, which are in every way similar, occur in at least some cases of diabetes. These alterations are apparently produced by some general cause which acts on all of the glands belonging to this particular group.

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